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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,986	10/17/2003	Nancy Jean Britten	PC27098	1367

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PHARMACIA & UPJOHN
7000 Portage Road
KZO-300-104
KALAMAZOO, MI 49001

EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
04/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,986	BRITTEN ET AL.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,14-21,23-28 and 30-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 14-21, 23-28 and 30-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I (claims 1-40), election of ceftiofur hydrochloride as the antibacterial substance, election of Labrafil M-19944CS, which is a polyglycolized glyceride having oleic acid as the main fatty acid component, as the amphipathic oil, and cottonseed oil as the non-aqueous carrier in the reply filed on 2/28/08 is acknowledged. Applicants elect, with traverse, the mammary gland as the single organ. The traversal arguments have been addressed in the office action dated 4/21/08.

Prior art search indicated that the elected species of active ingredient Ceftiofur hydrochloride is not free of prior art. The prior art found has been applied in the rejections below.

Claims 1-4, 14-21, 23-28 and 30-40 are pending.

Claims 5-13, 22, 29 and 41-48 have been canceled.

Claims 1-4, 14-21, 23-28 and 30-40 are examined on the merit.

Applicant's amendment to claims 25, in the response filed on 1/21/09 has been acknowledged.

Any objections and/or rejections made in the previous office action dated 4/21/08 and not specifically discussed in original or modified form here are considered withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 21-26 and 30-40 remain rejected under 35 U.S.C. 102(b) as being anticipated by US 4,299,501 (Patil) as stated in the office action dated 10/280/08 and as reiterated below. Response to applicant's arguments appears at the end of the reiterated rejection.

In the instant invention applicants claim a pharmaceutical composition comprising (a) an amphipathic oil that is water dispersible and ethanol insoluble, (b) microcrystalline wax, and (c) a pharmaceutically acceptable non-aqueous carrier, stably dispersed therein an antibacterial substance in an antibacterially effective amount.

Patil discloses semisolid dispersion of pharmaceutical composition comprising pharmaceutical materials (column 3, lines 7-9), pegicol-5-oleate (amphipathic oil of the instant invention), mineral oil (non-aqueous carrier of the instant claim), microcrystalline wax (in examples 3 and 4). This reads on instant claims 1, 21 and 23-26. Since the instant claim 1 does not identify a specific antibacterial substance, the disclosure of active agent as pharmaceutical material reads on the limitation of instant claim 1. Patil further discloses sorbitan sesquioleate as an emulsifier (example 4) and hence reads on instant claim 39. Patil also discloses that the percentage of amphipathic oil , i.e., pegicol-5-oleate as 3% (in example 3) that is within the range recited in instant claims 30-32. Patil discloses that the percentage of microcrystalline wax

to be 10% (in example 4) that is within the range recited in instant claims 33-35. Patil discloses that the percentage of non-aqueous carrier, i.e., mineral oil as 25% (in example 4) that is within the range recited in instant claims 36-38. The disclosure of benzoic acid in example 3 reads on the instant claim 40 that recite benzoic acid.

Hence Patil anticipates instant invention as illustrated above.

Response to Arguments

Applicants argue that Patil discloses a process for preparing a semisolid dispersion that comprises of oil and water phases and the final product is an emulsion. Applicants further argue that the pharmaceutical active ingredient is optional and may be suspended in oil or aqueous phase. Applicants argue that the instant invention is a composition comprising an antibacterial substance dispersed in non-aqueous carrier and instant composition is not an emulsion. Applicants further state that the pharmaceutical material is present in the oil phase and there is no disclosure of an antibacterial substance dispersed in an oil carrier.

Applicant's arguments filed 1/21/09 have been fully considered but they are not persuasive. It should be noted that the instant claim 1 is drawn with a translational phrase "comprising" which is a open phrase that does not prevent additional ingredients being present in the composition including an aqueous phase. Because, the instant claim does not recite that the composition is aqueous free composition. It merely recites that the composition comprises of an amphipathic oil that is water dispersible and ethanol insoluble and the antibacterial substance is dispersed in an oil carrier. The disclosure of a pharmaceutical ingredient in the oil phase as stated in the rejection and as pointed out by the applicants in their instant response meets the limitations

of the instant claim as the instant claim does not specifically recite any antibacterial substance. Hence the rejection under anticipation by Patil is appropriate and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 14-21, 23-28 and 30-40 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,299,501 (Patil) in view of US 2002/0110561 A1 (Teagarden) as stated in the office action dated 10/280/08 and as reiterated below. Response to applicant's arguments appears at the end of the reiterated rejection.

Patil discloses semisolid dispersion of pharmaceutical composition comprising pharmaceutical materials (column 3, lines 7-9), pegicol-5-oleate (amphipathic oil of the instant invention), mineral oil (non-aqueous carrier of the instant claim), microcrystalline wax (in

examples 3 and 4). This reads on instant claims 1, 21 and 23-26. Since the instant claim 1 does not identify a specific antibacterial substance, the disclosure of active agent as pharmaceutical material reads on the limitation of instant claim 1. Patil further discloses sorbitan sesquioleate as an emulsifier (example 4) and hence reads on instant claim 39. Patil also discloses that the percentage of amphipathic oil , i.e., pegicol-5-oleate as 3% (in example 3) that is within the range recited in instant claims 30-32. Patil discloses that the percentage of microcrystalline wax to be 10% (in example 4) that is within the range recited in instant claims 33-35. Patil discloses that the percentage of non-aqueous carrier, i.e., mineral oil as 25% (in example 4) that is within the range recited in instant claims 36-38. The disclosure of benzoic acid in example 3 reads on the instant claim 40 that recite benzoic acid.

Patil does not teach ceftiofur hydrochloride (elected species of antibiotic substance) and the elected species of non-aqueous carrier cotton seed oil.

Teagarden teaches the composition comprising crystalline ceftiofur free acid (CCFA) (claim 11) and composition comprises of cottonseed oil (claim 8) that reads on instant claims 19 and 27. Teagarden also discloses mono-, di and tri-glycerides of fatty acid esters of oleic, linoleic, etc., the examples include non-oils such as polyethylene glycol (end of [0038] on page 3). This reads on the definition of instant claim 21 for the amphipathic oil and hence further reads on instant claims 23-26. Teagarden also discloses that the composition is used in a method of treating or preventing bacterial infection in mammals (claims 34-36). Teagarden further discloses that composition is suitable for parenteral subcutaneous and intra-mammary, intravenous administration and for topical applications ([0061]). Since the active ingredient is administered to mammary glands, it is obvious it is useful in treating mastitis, a bacterial

infection. This reads on instant claims 2 and 3. Teagarden further discloses that the composition can be administered subcutaneously to ears ([0063]) and hence reads on instant claim 4. Teagarden also disclose a therapeutically effective dosage of the ceftiofur ([0066]) and compositions containing 100 mg/ml (example 4), 200 mg/ml (example 2) and 300 mg/ml (example 7) that are well within the limits recited in the instant claims 16-18.

It would have been obvious to one skilled in the art to combine the teachings of Patil and Teagarden to arrive at the instant invention for a pharmaceutical composition comprising a vehicle that comprises (a) an amphipathic oil that is water dispersible and ethanol insoluble, (b) microcrystalline wax, and (c) a pharmaceutically acceptable non-aqueous carrier; said vehicle having stably dispersed therein an antibacterial substance in an antibacterially effective amount. Because, Patil teaches the use of microcrystalline wax, amphipathic oil and non-aqueous carrier for the preparation of compositions comprising pharmaceutical materials and Teagarden teaches the composition comprising the active ingredient ceftiofur free acid and cottonseed oil as the non-aqueous carrier. One would have been motivated to do so given the fact that Teagarden used the composition to treat bacterial infection of mammary glands and ear infection. Teagarden also discloses the importance of modification to carrier vehicle to make the in vivo performance of the bioactive substance controlled and predictable (page 5, column 1, [0066]). There would have been reasonable expectation success to modify the composition of cited references given the fact that the Teagarden teaches to modify the composition for mode of application, particular sites (organs) and organism being treated ([0065]).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12

USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

1. Applicants argue that office states that "Teagarden also discloses, mono-, di-, and triglycerides of fatty acids mid non-oils such as polyethylene glycol. The Examiner alleges that this reads on the definition of amphipathic oil. Applicants respectfully disagree with this statement. Polyethylene glycols are water soluble and thus are not amphipathic oils. Tri-glycerides are ordinary oils and fats. As anyone who has ever made a water in oil salad dressing by shaking the oil and water together knows the triglyceride oils are not readily dispersible in water. Accordingly, tri-glycerides are not amphipathic oils. Mono and di-glycerides are well known, emulsifiers, but are not known, to have the required water dispersibility and ethanol insolubility to be amphipathic oils. Teagarden does not disclose a composition of an antibacterial in a carrier containing an amphipathic oil. As set forth above the composition of Patil is an emulsion. When the emulsion of Pail is combined with composition of Teagarden the person skilled in the art would expect to obtain, some type of emulsion. Applicants' inventive

composition is a dispersion, not an emulsion. It is respectfully submitted that the combination of the teaching of Teagarden and Patil does not lead to Applicants' invention".

2. Applicants also argue that the instant invention is designed for releasing the active ingredient for a quick release and the effect of the active ingredient drops off quickly while the composition of Teagarden may be administered parenterally and is designed to provide the release of active ingredient on a sustained basis.

3. Applicants further argue quoting KSR stating that combination of the teachings of Patil and Teagarden does not lead to instant invention, because, Patil discloses a semisolid dispersion or emulsion and Teagarden discloses a sustained release drug suspension. Hence, there is no motivation for a person skilled in the art to combine the teachings to create a composition having rapid dispersibility which provides short milkout times after treatment.

Applicant's arguments filed 1/21/09 have been fully considered but they are not persuasive.

1. Applicants argument that "Teagarden also discloses, mono-, di-, and triglycerides of fatty acids mid non-oils such as polyethylene glycol, and polyethylene glycols are water soluble and are not amphipathic oils" is not persuasive. The reference to triglycerides and polyethylene glycol was made with reference to limitations in the instant claim 21. The instant claim 21 recite that "the amphipathic oil is a polyglycolized glyceride prepared by an alcoholosis reaction of natural triglycerides with polyethylene glycols". Teagarden discloses many triglyceride esters that are both aqueous, non aqueous and mixtures of both wherein one or more hydroxyl moieties of glycerol is esterified with fatty acid or polymers such as polyethylene glycol [0038]. As disclosed in [0038], "It is understood that the tri-glyceride vehicle may include the mono-,

di-, or triglyceryl ester of the fatty acids or mixed glycerides and/or propylene glycol di-esters **wherein at least one molecule of glycerol has been esterified with fatty acids of varying carbon atom length**. Some non-limiting examples of "non-oils" include polyethylene glycol (PEG) and aqueous based vehicles". This clearly illustrates that the glycerol is esterified with both fatty acid chains and polyethylene glycol chains and the resulting molecule is a amphipathic molecule with polar head group and a hydrophobic tail characteristic of an amphipathic molecule. However, if all the three hydroxyl groups are esterified with PEG then the molecule will be hydrophilic as applicants stated. As stated in the Teagarden [0038], **at least one molecule of glycerol has been esterified with fatty acids of varying carbon atom length.** Hence the molecule will be an amphipathic molecule. With regards to applicant's argument that the instant invention is composition which is a dispersion and that of the cited art is emulsion is also not persuasive. Because, the instant claim only recites that the "antibacterial substance is dispersed therein". The claim per se does not recite that the resulting composition is not an emulsion.

2. With regards to applicants argument that the instant invention is designed for releasing the active ingredient for a quick release and the effect of the active ingredient drops off quickly while the composition of Teagarden may be administered parenterally and is designed to provide the release of active ingredient on a sustained basis is also not persuasive. The claim as presented does not recite that the instant composition is designed for instant release of active ingredient and is not a delayed release formulation.

3. With regards, applicant's reference to KSR, it should be noted that "KSR forecloses the argument that a specific **t**eaching, **s**uggestion or **m**otivation (TSM) is required to support a

finding of obviousness". In the instant obviousness rejection office has used TSM analysis and has not KSR case law.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-4, 14-21, 23-28 and 30-40 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 30, 32, 34-36, 38-40, 49-66 of copending Application No. 10/795,191. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present invention is drawn to a pharmaceutical composition comprising a vehicle that comprises an amphipathic oil that is water dispersible and ethanol insoluble, microcrystalline wax, and a non-aqueous carrier, with an antibacterial agent. The claims of Application No. 10/795,191 are drawn to a pharmaceutical composition comprising a vehicle that comprises an amphipathic oil that is water dispersible and

ethanol insoluble, microcrystalline wax, and a non-aqueous carrier, with an antibacterial agent and a second agent selected from the group consisting of anti-inflammatory agents, analgesics and antipyretics. The claims of Application No. 10/795,191 are obvious over the present invention because the claims of the instant invention are drawn to active agents being an antibacterial agent and are drawn with the transitional phrase "comprising" that does not preclude other agents being present in the composition. Therefore, the claims of the present invention which can comprise an antibacterial agent an anti-inflammatory agents, analgesics or antipyretics and hence reads on the claims of the copending application 10,795,191.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's state that the rejections are premature and the pending claims in the copending application US 10/795,191 has not been indicated as being allowable. Applicants further state that should any of the pending claims in the copending application US 10/795,191 be allowed and not subject to restriction, applicants would be willing to consider filing a Terminal disclaimer if appropriate.

Applicant's arguments filed 1/21/09 have been fully considered but they are not persuasive. The double patenting rejection will be maintained until such time allowable subject matter is indicated in the instant application and the instant claims will be further evaluated with the pending claims in the copending application US 10/795,191 during the prosecution.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). Applicant's amendment to instant claim 25 and the arguments presented in reply to non-final action dated 10/28/08 does not over come the pending/maintained rejections.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654

/Andrew D Kosar/
Primary Examiner, Art Unit 1654